

**FREEDOM OF INFORMATION SUMMARY  
FOR  
COMPONENT<sup>®</sup> E-S & COMPONENT<sup>®</sup> E-C  
(Progesterone and Estradiol Benzoate)**

JUL 20 1999

**1. GENERAL INFORMATION**

NADA Number: 110-315

Sponsor: Ivy Laboratories  
Division of Ivy Animal Health, Inc.  
8857 Bond Street  
Overland Park, KS 66214

Generic Name: Progesterone, Estradiol Benzoate, and Tylosin Tartrate

Trade Name: Component<sup>®</sup> E-S with Tylan<sup>®</sup>; Component<sup>®</sup> E-C with Tylan<sup>®</sup>

Marketing Status: Over-the-counter (OTC)

Effect of Supplement: This supplement provides for the addition of a tylosin tartrate pellet as a local antibacterial to Component<sup>®</sup> E-S and Component<sup>®</sup> E-C.

**2. INDICATIONS FOR USE**

*Component<sup>®</sup> E-S with Tylan<sup>®</sup>*: For increased rate of weight gain and improved feed efficiency in steers weighing 400 lbs or more. *Component<sup>®</sup> E-C with Tylan<sup>®</sup>*: For increased rate of weight gain in suckling beef calves up to 400 lbs body weight.

**3. DOSAGE FORM(S), ROUTE OF ADMINISTRATION, AND RECOMMENDED DOSAGE**

Dosage Form: Implantation

Route of Administration: Subcutaneous implantation on the posterior aspect of the middle one-third of the ear by means of an implant gun.

Recommended Dosage: *Component<sup>®</sup> E-S with Tylan<sup>®</sup>*: One implant containing 200 mg progesterone, 20 mg estradiol benzoate, and 29 mg tylosin tartrate. *Component<sup>®</sup> E-C with Tylan<sup>®</sup>*: One implant containing 100 mg progesterone, 10 mg estradiol benzoate, and 29 mg tylosin tartrate.

NADA 110-315

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#### **4. EFFECTIVENESS**

The effectiveness requirement for this supplemental new animal drug application, with the indications for use and dosage as given in Sections 2 and 3 above, is met by utilizing the existing database in NADA 110-315 and conducting the additional adequate and well-controlled study included in this supplemental application.

##### **Pivotal Study:**

A study was conducted by William Barton, CAVL, Inc, Amarillo, TX, to evaluate the effectiveness of Component<sup>®</sup> E-S with Tylan<sup>®</sup> to lower the incidence of ear abscess formation. An implant site abscess induction model was developed to reliably create a high abscess rate in test animals. This model was used to test the ability of a tylosin tartrate pellet to reduce implant site abscess incidence in animals expected to develop an ear abscess. In the study, 40 beef steers were subjected to the abscess-inducing culture at the same time they were implanted with either Component<sup>®</sup> E-S with a Tylan<sup>®</sup> pellet or Component<sup>®</sup> E-S alone. Implant sites were observed at regular intervals up to 35 days following implantation. Abscess rate at each time point was significantly lower ( $P < 0.001$ ) in steers treated with Component<sup>®</sup> E-S with a Tylan<sup>®</sup> pellet compared to steers treated with Component<sup>®</sup> E-S alone, with the maximum incidence of abscesses of 8% and 94%, respectively.

#### **5. TARGET ANIMAL SAFETY**

Target animal safety of Component<sup>®</sup> E-S and Component<sup>®</sup> E-C is established by data in the parent application. The data provided in the effectiveness study described above was sufficient to conclude that the use of the tylosin pellet was safe for use in cattle. No further studies were required.

#### **6. HUMAN SAFETY**

Human safety is established for Component<sup>®</sup> E-S and Component<sup>®</sup> E-C by data in the parent application. No further studies were required for use of the tylosin pellet.

#### **7. AGENCY CONCLUSIONS**

Adequate data demonstrates the safe and effective use of a tylosin tartrate pellet added to Component<sup>®</sup> E-S and Component<sup>®</sup> E-C as a local antibacterial.

Under the Center's supplemental approval policy (21 CFR 514.106(b)(2)), this is a Category II change providing for the addition of a tylosin tartrate pellet as a local antibacterial to Component<sup>®</sup> E-S and Component<sup>®</sup> E-C. The approval of this change is not expected to have any adverse effect on the safety or effectiveness of this new animal drug. Accordingly, this approval did not require a reevaluation of the safety and effectiveness data in the parent application.

## 8. LABELING

Facsimile labeling is attached as follows:

1. Component<sup>®</sup> E-S with Tylan<sup>®</sup> Box Label
2. Component<sup>®</sup> E-S with Tylan<sup>®</sup> 20 Dose Foil Pouch
3. Component<sup>®</sup> E-S with Tylan<sup>®</sup> Package Insert
4. Component<sup>®</sup> E-C with Tylan<sup>®</sup> Box Label
5. Component<sup>®</sup> E-C with Tylan<sup>®</sup> 20 Dose Foil Pouch
6. Component<sup>®</sup> E-C with Tylan<sup>®</sup> Package Insert

**RESTRICTED DRUG – USE ONLY AS DIRECTED (CALIFORNIA) - FOR USE IN ANIMALS ONLY  
NOT FOR HUMAN USE – KEEP OUT OF REACH OF CHILDREN**

**Important:** Read enclosed instruction brochure and follow directions.

**Store at controlled room temperature – 15°-30°C (59°-86°F). DO NOT refrigerate – avoid excessive heat and humidity.**

# **COMPONENT® E-S**

BRAND IMPLANTS STEER IMPLANTS

progesterone USP 200 mg and estradiol benzoate 20 mg  
with 29 mg tylosin tartrate as a local antibacterial



COMPONENT® E-S Implants are for use in steers weighing 400 lbs. or more. Daily weight gains of up to 3 lbs. per animal can be expected in steers implanted with COMPONENT® E-S when fed a balanced high energy finishing ration. Maximum benefits of accelerated weight gains and improved feed efficiency will be obtained when implanting high quality animals free of feedlot diseases and parasitism.

**Contains:** 5 Cartridge Belts\* of 20 implants each. Each dose consists of progesterone USP 200 mg and estradiol benzoate 20 mg with 29 mg tylosin tartrate as a local antibacterial.

\* Patented by Ivy Laboratories, Inc. NADA 110-315, Approved by FDA

**100 IMPLANTS**



**WARNING:** Implant one dose - 9 pellets (entire contents of one cartridge) - in the ear subcutaneously. Any other site of implantation is in violation of Federal Law. DO NOT attempt to salvage implantation site for animal feed or human food.

**Caution:** Bulling, rectal prolapse, ventral edema and elevated tail-heads have occasionally been reported in animals implanted with progesterone and estradiol benzoate.

**Important:** Read the enclosed instruction brochure. Use as illustrated with a CAREFUL CLEAN TECHNIQUE. Never take short cuts at the expense of CLEANLINESS.

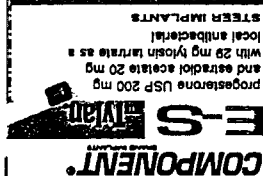
**Manufactured by a non-sterilizing process.**

COMPONENT is a registered trademark of Ivy Laboratories, Inc.

Tylan is a registered trademark of Eli Lilly and Company.

Manufactured for: VetLife L.L.C., Overland Park, KS 66214, USA by Ivy Laboratories, Inc.

01 21 03 00



100 DOSES CARTON  
REDUCED TO 75%

Front Panel



Bleed 1 color only

**COMPONENT<sup>®</sup> E-S**  
BRAND IMPLANTS STEER IMPLANTS

progesterone USP 200 mg and estradiol benzoate 20 mg  
with 29 mg tylosin tartrate as a local antibacterial

Bleed 1 color only



TEAR HERE

Fold & Seal Area Print Optional

COMPONENT<sup>®</sup> E-S Implants are for use in steers weighing 400 lbs. or more. Daily weight gains of up to 3 lbs. per animal can be expected in steers implanted with COMPONENT<sup>®</sup> E-S when fed a balanced high energy finishing ration. Maximum benefits of accelerated weight gains and improved feed efficiency will be obtained when implanting high quality animals free of feedlot diseases and parasitism.

**Contains:** One Cartridge Belt\* of 20 implants each sealed in a sanitary foil pouch. Each dose consists of progesterone USP 200 mg and estradiol benzoate 20 mg with 29 mg tylosin tartrate as a local antibacterial.

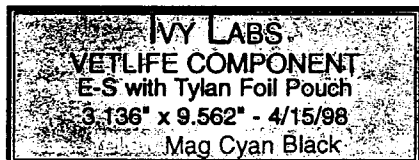
\* Patented by Ivy Laboratories, Inc. NADA 110-315, Approved by FDA



One 20-Dose Cartridge Belt

Bleed 1 color only

Bleed 1 color only



- 01 Black
- 02 Cyan
- 03 Magenta
- 04 Yellow
- 05 Special
- 06 Special
- 07 Black Stop

Fold & Seal Area Print Optional

Back Panel



Bleed 1 color only

Bleed 1 color only

**WARNING:** Implant one dose - 9 pellets (entire contents of one cartridge) - in the ear subcutaneously. Any other site of implantation is in violation of Federal Law. DO NOT attempt to salvage implantation site for animal feed or human food.

Caution: Bulling, rectal prolapse, ventral edema and elevated tail-heads have occasionally been reported in animals implanted with progesterone and estradiol benzoate.

Important: Read the enclosed instruction brochure. Use as illustrated with a CAREFUL CLEAN TECHNIQUE. Never take short cuts at the expense of CLEANLINESS.

**RESTRICTED DRUG - USE ONLY AS DIRECTED (CALIFORNIA) - FOR USE IN ANIMALS ONLY**  
**NOT FOR HUMAN USE - KEEP OUT OF REACH OF CHILDREN**

Store at controlled room temperature - 15°-30°C (59°-86°F).  
 DO NOT refrigerate - avoid excessive heat and humidity.

Manufactured by a non-sterilizing process.

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Tylan is a registered trademark of Eli Lilly and Company.

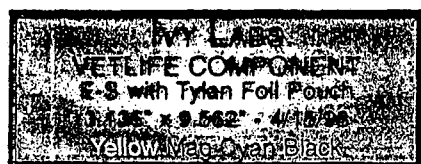
Manufactured for: VetLife L.L.C., Overland Park, KS 66214, USA by Ivy Laboratories, Inc.

01 21 02 00



Bleed 1 color only

Bleed 1 color only



20 DOSES FOIL POUCH  
 BACK

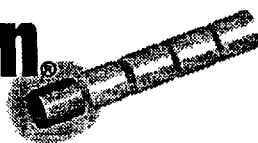
Fold & Seal Area Print Optional



TEAR HERE

**COMPONENT®**  
BRAND IMPLANTS**VetLife****E-S WITH Tylan®**

STEER IMPLANTS



progesterone USP 200 mg and  
estradiol benzoate 20 mg with 29 mg tylosin  
tartrate as a local antibacterial

**20 dose CARTRIDGE BELT\***

For use with the COMPONENT® One Gun™\*\*  
For Use In Animals Only

Each CARTRIDGE BELT holds 20 doses of COMPONENT® E-S Implants. Each dose of 9 pellets consists of 8 pellets containing a total of 200 mg progesterone USP and 20 mg estradiol benzoate plus 1 pellet containing 29 mg tylosin tartrate as a local antibacterial. COMPONENT® E-S Implants are recommended for use in steers weighing 400 lbs or more for INCREASED RATE OF WEIGHT GAIN AND FEED EFFICIENCY.

Manufactured by a non-sterilizing process.

**GENERAL INSTRUCTIONS:**

Study the Instructions which should be followed carefully at all times, avoiding short cuts. Skin infection can be avoided by properly preparing implant site and implanter. During fly season use fly repellent on implant site. One designated team member should always do the implanting. Cleanliness of hands and instruments is important at all times.

**WARNING**

Implant pellets in ear only. Any other site is in violation of Federal Law. Do not attempt to salvage implant site for animal feed or human use.

**KEEP THIS AND ALL OTHER DRUGS OUT  
OF REACH OF CHILDREN**

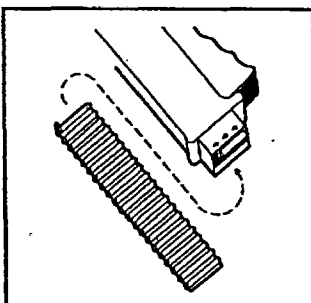
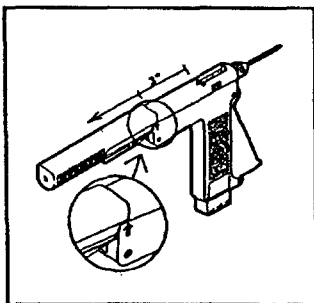
Restricted Drug—Use Only As Directed (California)

**CAUTION:**

Bulling, rectal prolapse, ventral edema and elevated tail-heads have occasionally been reported in animals implanted with progesterone and estradiol benzoate.

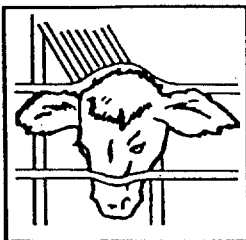
**IMPLANTING INSTRUCTIONS:****Loading the Implanter**

Load the Implanter following the instructions supplied with each Implanter



**Restrain the Animal**

Speed of implantation as well as safety of handlers is best achieved by restraining animal in a squeeze chute using head restraint. When implanting horned cattle, better control is obtained with additional use of nose tongs.

**Prepare the Implant Site**

Scrub the back side of the ear (implant site) with a piece of clean absorbent cotton which has been soaked with topical germicidal solution. Follow manufacturer's directions on germicide for correct strength and preparation of solution. Avoid getting into animal's eyes.

**Where to Implant**

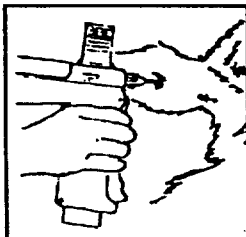
The full contents of the cartridge should be implanted beneath the skin on the back side of the middle one-third of the ear as illustrated in the drawing. The implant must not be closer to the head than the edge of the auricular cartilage ring farthest from the head. The location for insertion of the needle is a point toward the tip of the ear and at least a needle length away from the intended deposition site.



Avoid injuring the large arteries, veins and cartilage of the ear.

**Insert the Needle**

With one hand firmly grasp the ear. With other hand insert needle point through the skin and ease forward on a lateral plane until the entire length of the needle is under the skin.

**Implant the Pellets**

After inserting the needle fully in the correct implant position squeeze the trigger fully. As the needle is withdrawn from the ear, the controlled-pressure plunger action properly deposits the implant in the needle track. This procedure should prevent breakage or crushing of pellets if otherwise forced into contact with tough fibrous-tissue underlying the skin. The length and total contact area of a single dose are designed to permit absorption of the hormones after implantation to stimulate good weight gain. Broken or crushed pellets may interfere with rates of gain and may lead to undesirable side effects such as noted in the CAUTION.

**Clean the Needle**

Clean the planter needle with alcohol or a properly diluted germicidal solution prior to implanting the next animal.

Store at controlled room temperature 15° to 30° C (59° to 86° F)  
DO NOT refrigerate – avoid excessive heat and humidity.

NADA 110-315, Approved by FDA

\*U.S. Patent No. 4,531,938

\*\*U.S. Patent Nos. 4,762,515 & 5,522,797 – Ivy Animal Health, Inc.

COMPONENT E-S with Tylan is covered by U.S. Patent No. 5,874,098

COMPONENT is a registered trademark of Ivy Animal Health, Inc.

Tylan is a registered trademark of Eli Lilly and Company.

Manufactured for VetLife by Ivy Laboratories.

Overland Park, KS 66214, USA

VetLife and Ivy Laboratories are divisions of Ivy Animal Health, Inc.

01 21 01 00



**RESTRICTED DRUG – USE ONLY AS DIRECTED (CALIFORNIA) - FOR USE IN ANIMALS ONLY**  
**NOT FOR HUMAN USE – KEEP OUT OF REACH OF CHILDREN - FOR USE IN SUCKLING BEEF CALVES ONLY**

Progesterone and estradiol benzoate are naturally occurring hormones found in all cattle. COMPONENT® E-C Implant pellets are made by combining the two chemically pure steroid hormones - progesterone USP 100 mg and estradiol benzoate 10 mg - into one single dose consisting of 4 individual pellets contained within a multi-dose cartridge belt. The formulation has been designed to furnish complementary quantities of each of the two hormones as a means of achieving weight gain.

**DO NOT USE IN BULL CALVES INTENDED FOR REPRODUCTION OR IN CALVES LESS THAN 45 DAYS OLD.**

**Store at controlled room temperature – 15°-30°C (59°-86°F). DO NOT refrigerate – avoid excessive heat and humidity.**

## **COMPONENT® E-C**

BRAND IMPLANTS CALF IMPLANTS

progesterone USP 100 mg and estradiol benzoate 10 mg  
with 29 mg tylosin tartrate as a local antibacterial



Indicated for increased rate of weight gain in suckling beef calves up to approximately 400 lbs. of body weight.

**Contains:** 5 Cartridge Belts\* of 20 implants each. Packaged and sealed in a sanitary foil pouch. Each implant contains 5 pellets with a total content of progesterone USP 100 mg and estradiol benzoate 10 mg with 29 mg tylosin tartrate as local antibacterial.

\* Patented by Ivy Laboratories, Inc. NADA 110-315, Approved by FDA

100 IMPLANTS



**WARNING:** implant one dose - 5 pellets (entire contents of one cartridge) - in the ear subcutaneously. Any other site of implantation is in violation of Federal Law. DO NOT attempt to salvage implantation site for animal feed or human food.

**Caution:** Bulling, rectal prolapse, ventral edema and elevated tail-heads have occasionally been reported in animals implanted with progesterone and estradiol benzoate.

**Important:** Read the enclosed instruction brochure. Use as illustrated with a CAREFUL CLEAN TECHNIQUE. Never take short cuts at the expense of CLEANLINESS.

**Manufactured by a non-sterilizing process.**

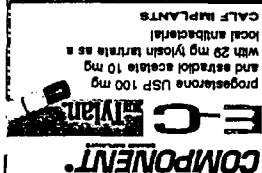
COMPONENT® E-C implants are safe when used fully in accordance with directions.

COMPONENT is a registered trademark of Ivy Laboratories, Inc.

Tylan is a registered trademark of Eli Lilly and Company.

Manufactured for: VetLife L.L.C., Overland Park, KS 66214, USA by Ivy Laboratories, Inc.

01 23 03 00



100 DOSES CARTON  
REDUCED TO 75%

Front Panel



Bleed 1 color only

**COMPONENT<sup>®</sup>** **E-C**  
BRAND IMPLANTS CALF IMPLANTS

progesterone USP 100 mg and estradiol benzoate 10 mg  
with 29 mg tylosin tartrate as a local antibacterial

Bleed 1 color only



Fold &amp; Seal Area Print Optional

TEAR HERE

Indicated for increased rate of weight gain in suckling beef calves up to approximately 400 lbs. of body weight.

**Contains:** One Cartridge Belt\* of 20 implants each sealed in a sanitary foil pouch. Packaged and sealed in a sanitary foil pouch. Each implant contains 5 pellets with a total content of progesterone USP 100 mg and estradiol benzoate 10 mg with 29 mg tylosin tartrate as local antibacterial.

\* Patented by Ivy Laboratories, Inc. NADA 110-315, Approved by FDA



One 20-Dose Cartridge Belt

Bleed 1 color only

Bleed 1 color only

IVY LABS  
VETLIFE COMPONENT  
E-C with Tylan Foil Pouch  
3.136" x 9.562" - 4/15/98  
Mag Cyan Black



Fold &amp; Seal Area Print Optional

- 1 Black
- 2 Cyan
- 3 Mag
- 4 Yellow
- 5 Spc
- 6 Spc
- 7 Stop
- 8 SPECIAL
- 9 SPECIAL
- 10 BLACK STOP

# Back Panel



Bleed 1 color only

Bleed 1 color only

**WARNING:** Implant one dose - 5 pellets (entire contents of one cartridge) - in the ear subcutaneously. Any other site of implantation is in violation of Federal Law. DO NOT attempt to salvage implantation site for animal feed or human food.

Caution: Bulling, rectal prolapse, ventral edema and elevated tail-heads have occasionally been reported in animals implanted with progesterone and estradiol benzoate. DO NOT USE IN BULL CALVES INTENDED FOR REPRODUCTION OR IN CALVES LESS THAN 45 DAYS OLD.

**RESTRICTED DRUG - USE ONLY AS DIRECTED (CALIFORNIA) - FOR USE IN ANIMALS ONLY  
NOT FOR HUMAN USE - KEEP OUT OF REACH OF CHILDREN - FOR USE IN SUCKLING BEEF CALVES ONLY**

Store at controlled room temperature - 15°-30°C (59°-86°F).

DO NOT refrigerate - avoid excessive heat and humidity. Important: Read the enclosed instruction brochure. Use as illustrated with a CAREFUL CLEAN TECHNIQUE. Never take short cuts at the expense of CLEANLINESS.

Manufactured by a non-sterilizing process.

COMPONENT® E-C Implants are safe when used fully in accordance with directions.

COMPONENT is a registered trademark of Ivy Laboratories, Inc.

Tylan is a registered trademark of Eli Lilly and Company.

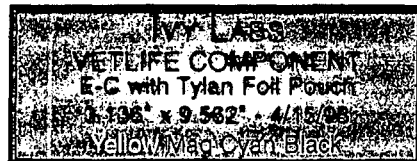
Manufactured for: VetLife L.L.C., Overland Park, KS 66214, USA by Ivy Laboratories, Inc.

01 23 02 00

PURCHASE SEAL  
20 IMPLANTS

Bleed 1 color only

Bleed 1 color only



Fold & Seal Area Print Optional

TEAR HERE

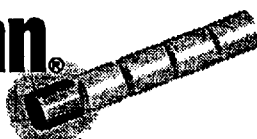
20 DOSES FOIL POUCH  
BACK

**COMPONENT®**  
BRAND IMPLANTS

**VetLife**

**E-C WITH Tylan®**

CALF IMPLANTS



progesterone USP 100 mg and estradiol benzoate 10 mg with 29 mg tylosin tartrate as a local antibacterial

## 20 dose CARTRIDGE BELT\*

For use with the COMPONENT® One Gun™\*\*  
For Use In Animals Only

Each CARTRIDGE BELT holds 20 doses of COMPONENT® E-C Implants. Each dose of 5 pellets consists of 4 pellets containing a total of 100 mg progesterone USP and 10 mg estradiol benzoate plus 1 pellet containing 29 mg tylosin tartrate as a local antibacterial. COMPONENT® E-C Implants are indicated for increased rate of weight gain in suckling beef calves up to approximately 400 lbs of body weight.

Manufactured by a non-sterilizing process.

### GENERAL INSTRUCTIONS:

Study the instructions which should be followed carefully at all times, avoiding short cuts. Skin infection can be avoided by properly preparing implant site and implanter. During fly season use fly repellent on implant site. One designated team member should always do the implanting. Cleanliness of hands and instruments is important at all times.

**DO NOT USE IN BULL CALVES INTENDED FOR REPRODUCTION, OR IN CALVES LESS THAN 45 DAYS OLD.**

### WARNING

Implant pellets in ear only. Any other site is in violation of Federal Law. Do NOT attempt to salvage implant site for animal feed or human use.

**KEEP THIS AND ALL OTHER DRUGS  
OUT OF REACH OF CHILDREN.**

Restricted Drug-Use Only As Directed (California)

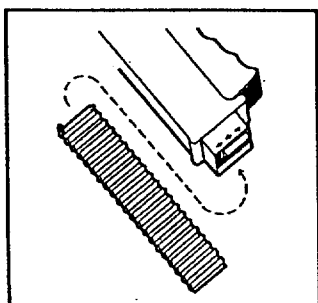
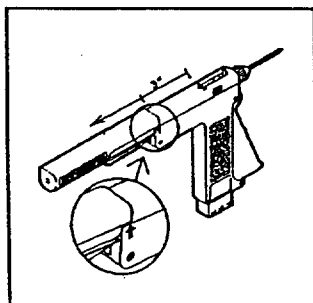
### CAUTION:

Bulling, rectal prolapse, ventral edema and elevated tail-heads have occasionally been reported in animals implanted with progesterone and estradiol benzoate.

### Implanter Instructions:

#### Loading the Implanter

Load the Implanter following the instructions supplied with each implanter.



#### Restrain the Animal

Speed of implantation as well as safety of handlers is best achieved by restraining animal in a squeeze chute using head restraint.

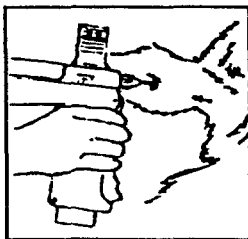


#### Prepare the Implant Site

Scrub the back side of the ear (implant site) with a piece of clean absorbent cotton which has been soaked with topical germicidal solution. Follow manufacturer's directions on germicide for correct strength and preparation of solution. Avoid getting into animal's eyes.

#### Where to Implant

The full contents should be implanted beneath the skin on the back side of the



middle one-third of the ear as illustrated in the drawing. The implant must not be closer to the head than the edge of the auricular cartilage ring farthest from the head. The location for insertion of the needle is a point toward the tip of the ear and at least a needle length away from the intended deposition site. Avoid injuring the large arteries, veins and cartilage of the ear.

#### Insert the Needle

With one hand firmly grasp the ear. With the other hand insert needle point through the skin and ease forward on a lateral plane until the entire length of the needle is under the skin.

#### Implant the Pellets

After inserting the needle fully in the correct implant position, squeeze the trigger fully. As the needle is withdrawn from the ear, the controlled-pressure plunger action properly deposits the implant in the needle track. This procedure should prevent breakage or crushing of pellets if otherwise forced into contact with tough fibrous-tissue underlying the skin. The length and total contact area of a single dose are designed to permit absorption of the hormones after implantation to stimulate good weight gain. Broken or crushed pellets may interfere with rates of gain and may lead to undesirable side effects such as noted in the CAUTION.

#### Clean the Needle

Clean the implanter needle with alcohol or a properly diluted germicidal solution prior to implanting the next animal.

Store at controlled room temperature 15° to 30° C (59° to 86° F)  
DO NOT refrigerate – avoid excessive heat and humidity.

NADA 110-315, Approved by FDA

\*U.S. Patent No. 4,531,938

\*\*U.S. Patent Nos. 4,762,515 & 5,522,797 – Ivy Animal Health, Inc.

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Overland Park, KS 66214, USA

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